

## REMARKS

Claims 14-22 were pending and under consideration, with Claims 18, 21, and 22 withdrawn from further consideration as being drawn to non-elected species. With this Amendment, Claims 14-22 are being amended. No claims have been cancelled or added. Thus, after entry of this Amendment, Claims 14-22 remain pending and under consideration.

### **I. Amendments**

Claims 14 and 19 have been amended to refer to a “conjugate comprising conjugate members, wherein said conjugate members are other than an antibody and consists of folate joined to a selective member.” Support for the amendment is found in the specification at least on page 6, lines 4-10; page 7, lines 18 to page 8, line 14; and page 9, lines 8-10.

Claims 19 and 20 have been amended by insertion of “galactosyl epitope” to define the moiety on the selective member Gal  $\alpha$ 1-3 Gal  $\beta$ 1-4GlcNAc-R. Support is found in the specification on page 8, lines 15-20.

Claims 14-22 have been amended to delete “moiety” and insert “member” to provide proper antecedent basis. Support is found throughout the specification, for example, on page 7, lines 18-23.

For the above reasons, the amendments are supported by the specification and claims as originally filed, and thus do not present new matter. Entry into the application is therefore requested.

### **II. Rejections under 35 USC § 112 ¶ 1: written description**

Claims 14-17 and 19 stand rejected under 35 USC 112 ¶ 1 for alleged insufficient written description. Applicant respectfully traverses.

The essential purpose of the written description requirement is to show possession of the claimed invention as of the filing date as a *prima facie* date of the invention. See In re Smith, 178 USPQ2d 620, 630 (CCPA 1973). Thus, the specification is required to contain a statement that adequately describes the inventions as claimed. However, the claimed invention need not be

described in *ipsis verbis* in order to satisfy the written description requirement. See MPEP § 2163.02; see also In re Luckach, 169 USPQ 795 (CCPA 1973).

The specification on page 9, lines 8-10 provides that “member of the conjugate may be polypeptides, saccharides, lipids, nucleic acids, or naturally occurring or synthetic organic molecules *other than the molecules already described*.” On the preceding page 6, lines 4-7, the specification describes moieties that bind to a target cell as including immunoglobulins and fragments thereof, including anti-idiotypic antibodies. Further, the specification describes selective member as including anti-idiotypic antibodies that mimic the selective moiety (page 8, lines 10-14). By operation of the phrase “polypeptides . . . other than the molecules described above,” there is ample written description support for “conjugate members other than antibodies.” Accordingly, withdrawal of the rejection for lack of written description support is respectfully requested.

Claims 14-17 and 19 stand rejected under 35 USC 112 ¶ 1 for alleged insufficient written description for the R group in Gal  $\alpha$ 1-3 Gal  $\beta$ 1-4GlcNAc-R. Applicant respectfully traverses.

Claims 19 and 20 have been amended to recite that the selective member is the “galactosyl epitope” Gal  $\alpha$ 1-3 Gal  $\beta$ 1-4 GlcNAc-R. The art-recognized definition of “epitope” is a “site recognized by an antibody or an antigen receptor.” (See Janeway C.A. et al., *Immunobiology*, Garland Publishing, New York, NY (2001)). The R group does not constitute a limitation “galactosyl epitope” since it is not the structure defined as being bound by the corresponding antibody. Thus, requiring written description of sufficient number of R groups is beyond that required under the law:

An applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that applicant was in possession of the *claimed invention*, i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of characteristics.

See MPEP § 2163 (emphasis added). The defined limitation in the claim is the galactosyl epitope itself, which Applicant submits is known to the skilled artisan and adequately described in the disclosure and claims by reference to its specific structure.

Accordingly, Claims 19 and 20 are sufficiently supported. Withdrawal of the rejection under 35 USC 112 ¶ 1 is requested.

### **III Rejections under 35 USC § 102(e): anticipation**

Claim 20 stands rejected under 35 USC § 102(e) as being allegedly anticipated by Kranz, US Patent No. 5,547,668 as evidenced by Borrebaeck, *Immunology Today* 14(10):477-479 (1993). Applicant respectfully traverses the rejection.

Anticipation of a claim requires that the reference teach every element of the claims. See MPEP § 2131. Thus, “a claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference.” See Verdegaal Bros. v. Union Oil Co. of California, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

Kranz describes folate attached to an antibody, where the antibody is capable of binding to a receptor on an effector cell. Exemplified antibodies are anti-T cell receptor and anti-Fc receptor antibodies. The antibodies target the effector cells to tumor cells.

Claim 19 as amended, however, specifically excludes conjugate members that are antibodies (*e.g.*, immunoglobulins). An assertion of inherent anticipation by the chance presence of  $\alpha$ -gal moieties on an antibody is negated by the specific exclusion from the scope of Claim 19 any antibodies acting as part of the conjugate. As such, Kranz in view of the secondary reference of Borrebaeck does not anticipate Claim 19. Because Claim 20 depends from Claim 19, Kranz and Borrebaeck do not anticipate Claim 20 for at least the same reasons.

Accordingly, withdrawal of the rejection under 35 USC § 102(e) is respectfully requested.

### **IV Rejections under 35 USC § 103(a): obviousness**

Claims 14-17, 19 and 20 stand rejected under 35 USC § 103(a) as being allegedly obvious over Pouletty (EP 0510949) in view of Kranz et al. (US Patent No. 5,547,668) and Galili et al., *Blood* 82:2485-2493 (1993). Applicant respectfully traverses.

In rejecting claims under §103(a), the Patent Office bears the burden of establishing a *prima facie* case of obviousness. See MPEP § 2142. To establish a *prima facie* case, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the references or to combine their teachings. Second, there must be a reasonable expectation of success. Third, the prior art reference(s) must teach or suggest each and every limitation of the rejected claims. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not in applicant's disclosure. See In re Vaeck, 20 USPQ2d 1438 (Fed. Cir. 1991); see also MPEP §2142.

Pouletty is described as teaching a conjugate having a moiety that binds to a target on a cell and a selective moiety that binds to an endogenous effector, such as a naturally occurring antibody. Pouletty does not describe use of folate conjugated to a selective member to which the host has been previously sensitized or to which the host has natural immunity.

Kranz is described as teaching a conjugate of folate and an antibody that binds to an effector cell to stimulate killing of the target cell that binds to the folate. Since the antibody binds to a target on an effector cell, sensitizing a host against the antibody conjugated to the folate would prevent the antibody from binding to the effector cell and effectively negates the function of the antibody moiety in Kranz. In contrast, the instant claims recite that the selective member is an antigen to which the host has been previously sensitized or to which the host has natural immunity. Thus the combination of references proposed by the Patent Office changes the principle by which the conjugate in Kranz operates. In this regard, the MPEP at section 2143.01 provides

If the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims *prima facie* obvious.

As such, the combination offered is an improper basis to assert a case of *prima facie* obviousness.

Galili, which teaches a galactosyl epitope Gal  $\alpha$ 1-3 Gal $\beta$ 1-4 GlcNAc-R, and the presence of high levels of anti-Gal antibodies in normal blood, does not provide any additional

information by which to modify Kranz without changing the operability of the conjugate in Kranz. Thus, the references of Pouletty, Kranz, and Galili, either alone or in combination, fail to teach or suggest a conjugate of folate and a selective member to which a host has been previously sensitized or to which the host has natural immunity.

Based on the foregoing, it is submitted that a case of *prima facie* obviousness has not been established for the claimed conjugates. Accordingly, withdrawal of the rejection under 35 USC § 103(a) is respectfully requested.

#### **V Allowance of a Generic Claim: Consideration of Claims 18, 21, and 22**

Upon the allowance of a generic claim, Applicant is entitled to consideration of a reasonable number of additional species embraced by the allowed generic claim. Thus, should Claims 14 and 19 be found allowable, Applicant requests withdrawal of the restriction to the elected species and reconsideration of Claims 18, 21, and 22. See MPEP § 809.02(c).

#### **VI. Conclusion**

Applicant submits that Claims 14-22 satisfy all of the statutory requirements for patentability and are in condition for allowance. An early notification of the same is kindly solicited.

If, upon review, the Examiner feels there are additional outstanding issues, the Examiner is invited to call the undersigned attorney at telephone no. (415) 781-1989.

No fees beyond those included with this communication are believed due. However, the Commissioner is authorized to charge any additional required fees, or credit any overpayment to Dorsey & Whitney LLP Deposit Account No. 50-2319 (File No. 456840-00028; Docket No. A-55320-2)

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Respectfully submitted,

DORSEY & WHITNEY LLP

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By: 

Euk Y. Oh, Reg. No. 54,345 for

Todd A. Lorenz, Reg. No. 39,754

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**Customer No.: 32940**

DORSEY & WHITNEY LLP

Four Embarcadero Center, Suite 3400

San Francisco, CA 94111-4187

Telephone: (415) 781-1989

Fax No. (415) 398-3249